

IN THE SPECIFICATION

In CROSS REFERENCE TO RELATED APPLICATIONS, please amend as follows:

This is a divisional application of co-pending US Application No. 10/008,955 filed December 7, 2001, which is a continuation of US Application No. 09/403,910 filed October 27, 1999, which was a nationalized application of PCT Application No. ~~PCT/US98/0862~~ PCT/US98/08672 filed April 30, 1998, which claims priority to US Provisional Application No. 60/045,885 filed April 30, 1997, which are all incorporated herein by reference in their entirety.

Please amend the two paragraphs, starting at page 11, line 28 through page 12, line 10 as follows:

Figure 16. Not provided. ~~PCR analysis of NK-92, NK-92MI and NK-92CI for human IL-2 cDNA. DNA isolated from the parental NK-92 and from the NK-92MI and NK-92CI transfectants was subjected to PCR analysis with primers flanking the first exon of the human IL-2 gene. PCR products were resolved on a 2% agarose gel, stained with ethidium bromide and viewed on a UV Transilluminator (Panel A). DNA was transferred to a nylon membrane and analyzed by Southern blot analysis with a radiolabelled probe for the hIL-2 gene (Panel B).~~

Figure 17. Not provided. ~~Northern blot analysis of cytokine expression in NK-92, NK-92MI and NK-92CI. RNA samples isolated from the parental and transfected cell lines were separated by agarose gel electrophoresis blotted to nylon membrane by capillary transfer and hybridized with probes for human IL-2 (Panel A) and TNF- α (Panel B).~~

Please amend the three paragraphs starting at page 51, line 1 to page 52, line 11 to read as follows:

To confirm that NK-92MI and NK-92CI ~~have~~had in fact been transfected with hIL-2 gene, PCR analysis was performed on the parental and transfected cell lines. Primers flanking exon 1 of the hIL-2 gene, which has 88 base pairs (bp), were used to amplify DNA isolated from NK-92, NK-92MI and NK-92CI to assay for the presence of the genomic and cDNA forms. Agarose gel electrophoresis of the PCR products from the parental line revealed a single 263 bp fragment corresponding to the size expected for the DNA fragment

amplified from the genomic IL-2 gene (~~Figure 16, Panel A~~). However, analysis of both the NK-92MI and NK-92CI products revealed two bands, the 263 bp fragment corresponding to the genomic hIL-2 gene as well as a 175 bp fragment resulting from the amplification of the hIL-2 cDNA. To confirm the identity of these DNA fragments, Southern blot analysis with a radiolabeled probe specific for hIL-2 ~~probe~~ was performed. ~~As seen in Figure 16, Panel B, both~~ Both the 263 bp genomic fragment and the 175 bp cDNA fragment hybridized with the probe. These data indicate that both NK-92MI and NK-92CI had been successfully ~~transferred~~ transfected and ~~contain~~ contained the cDNA for hIL-2.

d. Analysis of Gene Expression. ~~To analyze expression~~ Expression of specific cytokines in the parental and transfected cell lines, ~~they~~ were analyzed by Northern blot analysis. RNA isolated ~~from~~ from the NK-92, NK-92MI, and NK-92CI cells was separated by electrophoresis, transferred to a nylon membrane and hybridized with probes for the cytokines hIL-2 and hTNF- α (~~see Figure 17~~). Northern blot analysis of IL-2 ~~in these cells~~ revealed that IL-2 RNA was not detectable in the parental cell line (~~Figure 17, Panel A, Lane 1~~). However, hIL-2 ~~was found in RNA from~~ was detected in both the NK-92MI and NK-92CI (~~Lanes 2 and 3, respectively~~). Two mRNA transcripts were detected in NK-92MI cells: ~~seen in NK-92MI~~, a major RNA species of approximately 1.9 kDa, and a less intense transcript at 2.4 kDa. In NK-92CI, a hIL-2 mRNA transcript of approximately 1.4 kDa was detected. ~~As well, a~~ A very faint band was also seen at 2.5 kDa. These data confirm that the transfected cells expressed IL-2 while the parental NK-92 cells did not. The significance of the multiple hIL-2 mRNA transcripts in the two transfectants is not clear, although it is possibly a consequence of the different vector constructs. Furthermore, in the case of NK-92MI, the integration of the hIL-2 gene into the genomic DNA may also have affected the RNA size.

TNF- α expression in ~~the~~ NK cells was also examined using this technique (~~Figure 17, Panel B~~). It ~~is~~ was seen that all three lines expressed the gene for this cytokine. A TNF- α probe hybridized to a 1.6 kDa band in RNA isolated from NK-92, NK-92MI and NK-92CI (~~Figure 17, Panel B~~). These results indicate that although transfection of NK-92 cells with the IL-2 gene resulted in expression of the IL-2 in the transfectants, this did not influence the expression of another cytokine.

IN THE DRAWINGS

Please enter the corrected drawing sheets for Figures 1-15, 18-20 and 21 and delete Figures 16 and 17 (originally Sheets 11 and 12).